(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
26 April 2001 (26.04.2001)

PCT

(10) International Publication Number
WO 01/29564 A1

(51) International Patent Classification[7]: G01N 33/68, 33/53, C07K 16/00, C12N 15/11, 15/12, 15/00, 15/63, A61K 38/17, 38/16, C12P 21/02

(21) International Application Number: PCT/US00/28066

(22) International Filing Date: 12 October 2000 (12.10.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/159,542	15 October 1999 (15.10.1999)	US
60/165,914	17 November 1999 (17.11.1999)	US
60/189,027	14 March 2000 (14.03.2000)	US

(71) Applicant *(for all designated States except US)*: **HUMAN GENOME SCIENCES, INC.** [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **RUBEN, Steven, M.** [US/US]; 18528 Heritage Hills Drive, Olney, MD 20832 (US). **SHI, Yanggu** [CN/US]; Apartment 102, 437 West Side Drive, Gaithersburg, MD 20878 (US). **YOUNG, Paul, E.** [US/US]; 122 Beckwith Street, Gaithersburg, MD 20878 (US). **NI, Jian** [US/US]; 5502 Manorfield Road, Rockville, MD 20853 (US).

(74) Agents: **HOOVER, Kenley, K.** et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *With international search report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/29564 A1

(54) Title: PROTEIN TYROSINE KINASE RECEPTOR POLYNUCLEOTIDES, POLYPEPTIDES, AND ANTIBODIES

(57) Abstract: The present invention relates to novel human PTK polypeptides and isolated nucleic acids containing the coding regions of the genes encoding such polypeptides. Also provided are vectors, host cells, antibodies, and recombinant methods for producing human PTK polypeptides. The invention further relates to diagnostic and therapeutic methods useful for diagnosing and treating disorders related to these novel human PTK polypeptides.

What Is Claimed Is:

1. An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

(a) the polynucleotide shown as SEQ ID NO:X or the polynucleotide encoded by a cDNA included in ATCC Deposit No:Z;

(b) a polynucleotide encoding a biologically active polypeptide fragment of SEQ ID NO:Y or a biologically active polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No:Z;

(c) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No:Z;

(d) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(c), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide comprises a nucleotide sequence encoding a soluble polypeptide.

3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in ATCC Deposit No:Z.

4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide comprises the entire nucleotide sequence of SEQ ID NO:X or a cDNA included in ATCC Deposit No:Z.

5. The isolated nucleic acid molecule of claim 2, wherein the polynucleotide is DNA.

6. The isolated nucleic acid molecule of claim 3, wherein the polynucleotide is RNA.

7. A vector comprising the isolated nucleic acid molecule of claim 1.

8. A host cell comprising the vector of claim 7.

9. A recombinant host cell comprising the nucleic acid molecule of claim 1 operably limited to a heterologous regulating element which controls gene expression.

10. A method of producing a polypeptide comprising expressing the encoded polypeptide from the host cell of claim 9 and recovering said polypeptide.

11. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

(a) the polypeptide shown as SEQ ID NO:Y or the polypeptide encoded by the cDNA;

(b) a polypeptide fragment of SEQ ID NO:Y or the polypeptide encoded by the cDNA;

(c) a polypeptide epitope of SEQ ID NO:Y or the polypeptide encoded by the cDNA; and

(d) a variant of SEQ ID NO:Y.

12. The isolated polypeptide of claim 11, comprising a polypeptide having SEQ ID NO:Y.

13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.

14. A recombinant host cell that expresses the isolated polypeptide of claim 11.

15. A method of making an isolated polypeptide comprising:

(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and

(b) recovering said polypeptide.

16. The polypeptide produced by claim 15.

17. A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

18. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

20. A method for identifying a binding partner to the polypeptide of claim 11 comprising:

(a) contacting the polypeptide of claim 11 with a binding partner; and

(b) determining whether the binding partner effects an activity of the polypeptide.

21. A method of screening for molecules which modify activities of the polypeptide of claim 11 comprising:

(a) contacting said polypeptide with a compound suspected of having agonist or antagonist activity; and

(a) assaying for activity of said polypeptide.